Author’s response to reviews

Title: Clinical impact of the perioperative management of oral anticoagulants in bleeding after colonic endoscopic mucosal resection

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Thank you for the thoughtful feedback you provided regarding our manuscript "Clinical impact of the perioperative management of oral anticoagulants in bleeding after colonic endoscopic mucosal resection". Point-by-point response to the reviewers' comments are as follows.

In reply to Reviewer 1 (Dr. Yosuke Tsuji)

1. Reviewer: The aim of this study might be elucidating the perioperative management of anticoagulants without HBT. Then, in order to investigate it, it is more appropriate to compare anticoagulants takers with HBT and those without HBT (continuous warfarin or one-day skip of DOACs). However, because of a small sample size, authors could not demonstrate a significant difference in post-EMR bleeding rate between those two groups and they compared a control group not taking antithrombotic agents with the other groups. This is an unignorable limitation.

Authors: We would like to thank the reviewer for the comments. Our data showed no significant differences in the bleeding rates between HBT group and without HBT (DOAC and warfarin) group because of small sample size and a little bit higher bleeding rates in the management of anticoagulants without HBT. We have corrected our aim and limitations.
In the revised paper, we have added the following sentence:

(Introduction section, line 18, page 5)

“We therefore investigated bleeding risk after colonic EMR in patients taking oral coagulants and evaluated whether the continuous use of warfarin and the one-day skip of DOACs could be eligible for perioperative management without HBT.

(Discussion section, line 12, page 14)

“There are several limitations in this study. First, this study was a retrospective study at a single institution with a small sample size. Furthermore, the superiority of the perioperative management of oral anticoagulants without HBT was not shown, and 

2. Reviewer: In Tables 3 and 4, it is difficult to know whether risk-per-polyp or risk-per-patient is treated. For example, Table 3 shows the number of HBT group is 31, but Table 4 showed 32. Please add an explanation.

Authors: We have corrected the number of HBT group in Table 4 (n = 31) and revised table 4 according to the reviewer 2’s comments.

In reply to Reviewer 2 (Dr. JX Yu)

1. Reviewer: The article needs significant editing for grammar and English fluency.

Authors: We would like to thank the reviewer for the comments. We received editing check from American Journal Editing (AJE) and revised our manuscript.

2. Reviewer: The methods section remains nebulous. For example - definition of the control group should be explicit in the text - were those patients on anything (antiplatelets?). Additionally, the authors do not specify which groups are being compared in their univariate and covariate analysis explicitly (for example, that anticoagulants were combined together).

Authors: We have revised the methods section and added the definition of each group.

In the revised paper, we have added the following sentence:

(Methods section, line 50, page 5)

“The patients were classified according to taking antithrombotic agents (only antiplatelets, only anticoagulants and both antiplatelets and anticoagulants), and the patients who did not use anticoagulants or antiplatelets were analysed as controls.”
3. Reviewer: How was the warfarin withdraw group analyzed - was this with the anticoagulant cohort or control cohort? Again this should be explicit in the text.

Authors: Warfarin withdraw group was analyzed as anticoagulants group but was excluded from continuous warfarin group in table 4.

4. Reviewer: Tables 1 and 2 present descriptive statistics of two cohorts - bleed vs. non-bleed however, it would be more useful to compare the descriptive statistics of the groups: control, HBT, continuous warfarin and one-day skip DOAC, similar to what is presented in the first 5 rows of table 3 as these are the cohorts being compared. They should then present their univariate and multivariate analysis separately with bleed as the main outcome. As GIB is the only outcome, this could be easily presented graphically with odds ratios w/ 95% CI on the X-axis and independent variables/covariates on the y-axis.

Authors: As the reviewer’s pointed out, we revised table 4 and made new table (table 5) that bleeding rates and risk ratios were shown.

In the revised paper, we have added the following sentence:

(Results section, line 53, page 10)

“The bleeding rates in the HBT group and continuous DOACs group were significantly higher than those in the control group (p < 0.05), and high bleeding risk ratios were calculated (table 5). However, there were no significant differences in bleeding risk between HBT and continuous warfarin or one-day skip DOACs.”

5. Reviewer: The strength of this paper is in the fact that the authors are able to capture actual anticoagulant use (ie continuous warfarin vs. HBT vs. 1-day doac cessation vs control), this results currently seem buried. The paper would be significantly strengthened if the univariate and multi-variate analysis were conducted using these cohorts as opposed to a combined anticoagulant cohort. If this cannot be done, they should be discussed both as a limitation and in their methods. Currently, the multivariate analysis as presented is redundant and confusing and may be simplified by just presenting the GIB rates of continuous warfarin/HBT/1day doac cessation vs control.

Author: We would like to thank the reviewer for the comments. As mentioned above, we have added table 5 showing bleeding rates and risk ratios according to management of anticoagulants (comparing continuous warfarin, HBT, one-day skip DOAC and control).

6. Reviewer: The authors conclude that 1-day DOAC skip would be clinically acceptable in patients as peri-operative management of patients not on HBT however this conclusion seems to be an over-reach as they do not have any patients who went from continuous warfarin to 1-day
skip DOAC especially as the authors themselves describe this study as a pilot study and it is not clear if patients were switched off warfarin to 1-day stop DOAC therapy. The conclusion should be rewritten with this in account.

Authors: As the reviewer’s pointed out, we have corrected our conclusions according to our further analysis.

In the revised paper, we have changed as follows:

(Discussion section, line 34, page 14)

“... and perioperative management of oral anticoagulants based on the shortest cessation without HBT did not prevent bleeding.”

In reply to Reviewer 3 (Dr. Takuya Yamada)

Minor points

1. Reviewer: P10L2; Please indicate the number of patients who took dabigatran, rivaroxaban, apixaban, and edoxaban.

Author: We have added the numbers of anticoagulants in the results section.

In the revised paper, we have added the following sentence:

(Discussion section, line 40, page 9)

“For anticoagulants, 34 patients used warfarin and 28 patients used DOAC (rivaroxaban n = 10, apixaban n = 9, edoxaban n = 5, dabigatran n = 4).”

2. Reviewer: P16L50; Please delete either 9th or 16th references.

Reviewer: We have deleted 9th and 16th references.

Again, thank you for giving us the opportunity to strengthen our manuscript with your valuable comments and queries.

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